(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 December 2003 (18.12.2003)

PCT

(10) International Publication Number
WO 2003/103577 A3

(51) International Patent Classification[7]: C07H 21/04, C07K 5/00, 14/00, C12N 15/63, 15/00

(21) International Application Number: PCT/US2003/017442

(22) International Filing Date: 4 June 2003 (04.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/386,932 6 June 2002 (06.06.2002) US

(71) Applicant and
(72) Inventor: WUN, Tze, Chein [US/US]; 613 Huntley Heights Drive, -, Ballwin, MO 63021-3020 (US).

(74) Agent: NEALEY, Tara, A.; Sonnenschein Nath & Rosenthal, Attention: IP Department - St. Louis Office, P.O. Box 061080, Wacker Drive Station - Sears Tower, Chicago, IL 60606-1080 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report: 4 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2003/103577 A3

(54) Title: NOVEL RECOMBINANT ANTICOAGULANT PROTEINS

(57) Abstract: Novel recombinant anticoagulation proteins, methods of their use and methods of their production are described. In particular, recombinant fusions of annexin V (ANV) and Kunitz protease inhibitors (KPI) that possess potent anticoagulant activity are provided. The fusions, abbreviated ANV:KPI, utilize ANV having high affinity for phosphatidyl-L-serine with various KPI's to target serine proteases in membrane-associated coagulation complexes in the blood coagulation cascade. ANV:KPIs are potentially useful antithrombotic drugs permitting localized passivation of thrombogenic vessel walls and associated thrombi.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/17442

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07H 21/04; C07K 5/00, 14/00; C12N 15/63, 15/00
US CL : 435/320.1, 325, 69.6; 514/2, 822; 530/300, 350; 536/23.4
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/320.1, 325, 69.6; 514/2, 822; 530/300, 350; 536/23.4

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JANG et al. Influence of Blockade at Specific Levels of the Coagulation Cascade on Restenosis in a Rabbit Atherosclerotic Femoral Artery Injury Model. Circulation. 15 November 1995, Vol. 92, pp. 3041-3050.	1-23
A	DENNIS et al. Kunitz Domain Inhibitors of Tissue Factor-Factor VIIa. J. Biol. Chem. 02 September 1994, Vol. 269, No. 35, pp. 22129-22136.	1-23
A	LEFKOVITS et al. Selective inhibition of factor Xa is more efficient than factor VII tissue factor complex blockade at facilitating coronary thrombolysis in the canine model. J. Am. Coll. Cardiol. December 1996, Vol. 28, No. 7, pp. 1858-1865.	1-23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
09 September 2003 (09.09.2003)

Date of mailing of the international search report
05 DEC 2003

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703)305-3230

Authorized officer
Holly Schnizer

Telephone No. (703 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

PCT/US03/17442

Continuation of B. FIELDS SEARCHED Item 3:
STN (Bioscience); EAST (all databases); Sequence search for SEQ ID NOs: 1-10; search terms: kunitz inhibitor, annexin V, TFPI, antistasin, ATS, Tick anticoagulant protein, TAP, ancylostoma caninum anticoagulant peptide (AcAP5, AcAP6, Kapp, fusion, Wun, Tze-Chein.